confirmation that the attached claims are the correct and pending claims is respectfully requested.

Claims 3 and 4 are understood to have been withdrawn from consideration. Claims 6-8 and 11-20 have also been withdrawn from consideration. Claims 1, 2, 5, 9 and 10 are rejected. No new matter is added. Claims 1, 2, 5, 9 and 10 are submitted for further consideration in view of the below remarks. Applicants respectfully request reconsideration and withdrawal of all rejections.

Claim Rejections - 35 U.S.C. 103

Claims 1-2, 9 and 10 are rejected under 35 USC §103 as being obvious over Merck Index #4852. It is alleged that it is known to use indomethacin and nitric oxide donors for incontinence, and it would be obvious to combine two compounds, each of which is taught as useful for the same purpose, in order to form a composition to be used for the same purpose.

Applicants respectfully disagree. Applicants wish to point out that in certain preferred embodiments, the claimed invention relates to compounds for use in the treatment of urinary incontinence, that exhibit a superior pharmacological profile as compared to other drugs known for use with this condition. That is, the claimed invention in certain embodiments is concerned with methods for the treatment of urinary incontinence by administering the nitro-oxy derivative of indomethacin, that is, (3-nitrooxymethyl)phenyl ester ("NO-indomethacin"), exhibiting a superior pharmacological profile.

Applicants respectfully urge that no such invention is taught or suggested in the prior art including the cited references. Applicants point out that starting at page 57 of the specification, Examples 11-12 and 11A-11D (comparison) disclose *in vitro* pharmacological experiments, wherein it has been investigated whether the pharmacological effect (relaxation of smooth muscle tissue) decreases with repeating dose administration (tachyphylaxis). Sample strips were obtained from pig urethral smooth muscle and subjected to a 10 mN tension and connected to a force transducer. The samples were then exposed to Krebs solution without Ca^{++}, to determine the maximum strip relaxation level (100% relaxation). After restoring normal tone to the sample strips by the addition of Krebs solution, relaxation effect for each of the test compounds was determined using a 10^{-5} molar quantity of the compound in solution. Two treatments were performed for each compound.

The results of the experiments are disclosed in Table 6, expressed as a percentage, considering 100% the highest relaxation determined by medium without Ca^{++} (See page 58 of the specification). Table 6 discloses the following results:

- Indomethacin is inactive, that is, it does not have any relaxing effect (Example 11A);
- The NO donors nitroglycerin and L-arginine have high relaxing activity but induce tachyphylaxis, since in the second run the relaxing effect was much lower (by at least about 45%) compared to the first run (Examples 11C and 11D);
- NO indomethacin has high relaxing activity and does not demonstrate tachyphylaxis, as activity is substantially the same in the first and second runs (Example 11B).

Applicants therefore urge that the results of Table 6 clearly demonstrate that the methods and compounds of the claimed invention are unexpectedly advantageous as compared to a mixture of NO-donors and indomethacin.

Moreover, Applicants wish to point out that in Table 6 (Example 12), it is demonstrated that the relaxing effect for the derivative NO-flufenamic acid (See formula at page 46) increases slightly from the first to second run. In this case, however, in contrast to the precursor indomethacin, the precursor flufenamic acid already possesses a myorelaxing activity (See Example 11B).

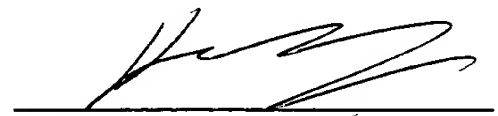
Applicants therefore urge that those of ordinary skill in the art could not have reasonably expected, on the basis of a combination of indomethacin and NO donors, to obtain a NO donor compound of indomethacin showing the following advantageous characteristic with respect to relaxing effect: 1) a high relaxing effect, wherein the precursor anti-inflammatory compound indomethacin displays no such activity, and 2) in contrast to NO-donors, constant drug effectiveness after repeated administration. Thus, in view of such unexpected and advantageous improvements, Applicants submit that the claimed invention can only be considered non-obvious over any known use of indomethacin and NO donors for incontinence. Applicants urge withdrawal of all rejections.

In view of the remarks above, Applicants respectfully submit that this application is in condition for allowance and request favorable action thereon.

In the event this paper is not considered to be timely filed, Applicants hereby petition for an appropriate extension of time. The fee for this extension may be charged to our Deposit Account No. 01-2300. The Commissioner is hereby authorized to charge

any fee deficiency or credit any overpayment associated with this communication to Deposit Account No. 01-2300, referencing Attorney Docket No. 108907-09002.

Respectfully submitted,



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HJC:ccd

Enclosure: Copy of pending claims 1, 2, 5, 9 and 10